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Disturbance of the Functional Activity of the Sympatic Adrenaral System and Processes of Lipid Peroxidation in Women of Fertile Age with Metabolic Syndrome

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Annotation: The aim of the given work was study interactions of impairments sympathetic – adrenal systems functional condition and processes of peroxidal oxidation of lipids in woman of fertile age with metabolic syndrome. 62 women at the age of 25-49 were observation. They were randomized into 3 groups: I (control) – 15 healthy persons, II – 22 patients with arterial hypertension, III – 25 women with arterial hypertension in combination with metabolic syndrome. The results of carried investigations showed that activation of sympathetic adrenal system and processes of peroxidal oxidation of lipids took place in metabolic syndrome. Marked lowering of sympathetic – adrenal system key ferment catecholamins (MAO monoaminooxidaze) desamidization activity and considerable activation of peroxidal oxidation of lipid products which have great significance in revealing the mechanism of metabolic syndrome development were observed in metabolic syndrome. This results in the prolonged toxic influence of catecholamins on myocardium.

Keywords: metabolic syndrome, sympathetic–adrenal system, catecholamins, arterial hypertension, insulinresistens.

Introduction

Interest in the study of metabolic syndrome (MS) in recent decades among specialists, scientists and practitioners, is associated with its significance as a precursor of type 2 diabetes mellitus and cardiovascular diseases caused by atherothrombogenic processes (1,5,10). In recent years, nevertheless, great importance is attached to humoral factors in the development of arterial hypertension (AH) and metabolic disorders: basal hyperinsulinemia, mediators of sympathetic activity and hormones of the renin-angiotensin-aldosterone system [2,3,12]. It has been established that in coronary heart disease (CHD) the level of monoamine oxidases (MAO) is reduced by 2 times, and in acute myocardial infarction by 2.5 times (6). At present, it is reliably known that the activation of peroxide free radical processes underlies the pathogenesis of many cardiovascular diseases. The processes of lipid peroxidation (LPO) lead to the accumulation of oxidized low-density lipoproteins (LDL), which leads to a violation of microcirculation. From this point of view, the study of LPO processes in MS has become especially interesting, since one of the main biochemical parameters of blood in this case is an increase in the level of biogenic amines in the blood [4,5,6,11]. Recent studies indicate that in order to understand atherosclerosis, hypertension and coronary heart disease, diabetes mellitus (DM), it is necessary to study biogenic amines (epinephrine, norepinephrine, serotonin, etc.) and their precursors, metabolic products and enzymes involved in their metabolism [3,5,8,9,12].

Purpose of work: To study the relationship between the functional state of the sympathetic-adrenal system (SAS) and the processes of lipid peroxidation in women of childbearing age with metabolic syndrome.

Material and Methods

In a hospital setting, 62 examined women aged 25-49 years were randomized into the following 3 groups: I (control) - healthy individuals aged 25-40 years - 15 people; II - patients with arterial hypertension - 22 people aged 29-49 years; Group III - patients with MS - 25 women aged 26-49 years.

The following methods were used to diagnose MS:

1. Determination of body mass index (BMI) was carried out according to the formula: weight (kg) / height (m)2. According to the WHO classification, body weight is considered overweight if the BMI exceeds 24.9.
2. Abdominal obesity was determined by measuring the waist circumference (WC) between the edge of the lower rib and the wing of the ilium. The following was taken as a physiological indicator: for women, less than 80 cm.
3. To determine metabolic disorders in patients, the levels of total cholesterol (Cholesterol), triglycerides, very low density lipoprotein cholesterol (VLDL), LDL cholesterol, high density lipoprotein cholesterol (HDL), atherogenic coefficient were studied (the lipid spectrum was determined biochemically with a biochemical express analyzer "Reflotron -Roche"), blood glucose (glucose oxidase method).
4. General clinical examination was carried out according to generally accepted programs (clinical analysis of blood, urine, ECG, X-ray examination of the chest, etc.).

Determination of adrenaline (A), norepinephrine (NA), dopamine (DA) and DOPA in daily urine was performed by trioxyindole fluorimetric method modified by E.Sh. Matlina, Z.M. Kiseleva, I.E. Sophieva. The content of catecholamine (CA) conjugates in urine was determined according to the method described by T.I. Lukicheva, V.V. Menshikov, T.D. Bolshakova. LPO products in the blood serum were determined by the method of B.V. Gavrilov et al., MAO in the blood - by the method of A.I. Balakleyevsky.

The results of clinical trials were processed using the application programs for statistical processing of the Excel program, as well as the method of variation statistics according to Fisher using t-tests of Student's tables. Differences between the arithmetic mean values were considered statistically significant at $p<0.05$ (G.G. Avtandilov).

Result and Discussion

The first table shows the average values and confidence intervals for the content of lipids, glucose and LPO products in the blood serum for all the examined groups at $t>2$ according to the Student's criterion ($P<0.05$; $P<0.01$; $P<0.001$). As can be seen from the table, the maximum level of total cholesterol, triglycerides, LDL and malondialdehyde (MDA - LPO product) is observed in group III, compared with the control and group II. Compared with the control, the value of total cholesterol in patients with hypertension increased by 47.7%, and in women with MS - by 56.8%. The content of triglycerides in group III exceeded the control value by 60%, in group II by 26.6%. The level of LDL in group II exceeded that of the control group by 66.6%, the content of LDL in group III increased by 98.7% compared with the healthy group. HDL in II and III groups is reduced in comparison with the control. When comparing the first and second groups, the difference in blood glucose levels was 14.6%, and in groups I and III - 56%. When analyzing the MDA data, we

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noted a statistically significant increase in the content in group III compared to group I by 102.2%, and the difference between groups I and II was 62.8%.

Table 1. The content of lipids, glucose and lipid peroxidation products in the blood serum of practically healthy people and patients with arterial hypertension and metabolic syndrome

Index	1st group	2nd group	3rd group
Total cholesterol, mmol/l	4,4±0,2	6,5±0,4***	6,9±0,4***
Triglycerides, mmol/l	1,5±0,2	1,9±0,1*	2,4±0,2**
LDL cholesterol, mmol/l	2,7±0,3	4,5±0,4**	5,4±0,4***
HDL cholesterol, mmol/l	1,3±0,1	1,1±0,1*	1,0±0,2*
VLDL cholesterol, mmol/l	0,3±0,2	0,4±0,2^	0,6±0,3^
Atherogenic index, units	2,9±0,2	3,8±0,4*	4,6±0,4***
MDA, nmol/ml	3,5±0,2	5,7±0,2***	7,1±0,4***
Fasting plasma glucose, mmol/l	4,1±0,2	4,7±0,2*	6,4±0,3***

Note. Cholesterol - cholesterol, LDL - low density lipoproteins, HDL - high density lipoproteins, VLDL - very low density lipoproteins, MDA - malonic dialdehyde. * - P<0.05; ** - P<0.01; *** - P<0.001; ^ - unreliable.

The second table shows the average values of daily urinary excretion of CA in all examined groups.

During the study, we noted a statistically significant increase in the excretion of A and NA in the daily urine of patients with AH and MS. Thus, the daily excretion of total A in hypertensive patients with healthy individuals increased by 40.9% (P<0.001), total NA by 32.2%. Excretion in the daily urine of all fractions of DA and DOPA in patients with hypertension is statistically significantly lower than the control level. The excretion of free, conjugated and total A and NA in patients with MS was statistically significantly higher than in healthy people (Table 2). The difference in DOPA excretion in MS was 29.8% (P<0.001) (Table 2).

In the third table, the results of the study of A and HA in the blood of healthy women and patients with hypertension and MS. When analyzing the indicators, we noted a significant increase in the content of A and NA in patients compared with the control group. Thus, the level of A in patients with MS was 3 times higher than in healthy people, and in patients with AH 1.5 times. The content of NA in the blood of patients with MS was increased by 2.7 times in the control group, and in comparison with the examined AH by 1.4 times. The study of MAO showed a statistically significant decrease in its level in groups II and III (P<0.001).

Table 2. Daily excretion of catecholamines in apparently healthy people and patients with metabolic syndrome

Groups	Catecholamines			
	A, mcg/day	NA, mcg/day	DA, mcg/day	MOA, mcg/day
I	St. 4,4±0,1 Кон. 3,9±0,1 Сум. 8,3±0,2	St. 9,8±0,4 Кон.9,1±0,3 Сум.18,9±0,5	St.295,4±9,2 Кон.174,5±5,4 Сум.469,9±6,1	48,0±0,6
II	St.5,8±0,3*** Кон.5,9±0,4 *** Сум11,7±0,3***	St.12,9±0,3*** Кон.12,1±0,2*** Сум.25,0±0,4***	St.163,2±4,5** Кон.166,5±5,1^ Сум.329,7±13,1***	56,5±0,8***
III	St. 9,7±0,4*** Кон.8,0±0,3*** Сум.17,7±0,4***	St.13,6±0,3*** Кон.12,5±0,2*** Сум.26,1±0,3***	St. 170,5±1,2*** Кон. 155,6±1,2* Сум. 326,1±21,5***	64,4±0,6***

Note. A - adrenaline, NA - norepinephrine, DA - dopamine, MAO - monoamine oxidase, St. - free, Con. - conjugated, Sum. - total. * - P<0.05; ** - P<0.01; *** - P<0.001; ^ - unreliable.

Table 3. The content of adrenaline and norepinephrine, and the activity of MAO in the blood of practically healthy people and patients with metabolic syndrome

Groups	Adrenaline, nmol/l	Norepinephrine, nmol/l	MAO, unit / ex.
I	0,8±0,2	2,76±0,3	0,08±0,002
II	1,6±0,3	5,24±0,2	0,054±0,0029
III	2,4±0,3	7,48±0,3	0,042±0,003
p-1-2	p<0,001	p<0,001	p<0,001
P-1-3	p<0,01	p<0,001	p<0,001
P-2-3	p<0,01	p<0,01	p<0,001

Thus, the results of the studies carried out showed that MS activates the SAS, expressed by an increase in the content of A and NA in the blood and CA excretion (A, NA, DA, DOPA). An increase in SAS activity at the stages of formation in MS can be regarded as compensatory [3]. A further increase in the tension of the SAS activity is aimed at mobilizing the body's internal reserves. However, at one of the stages of this process, the catabolic orientation of the effects of the SAS begins to manifest itself, and a further increase in the activity of which becomes one of the main elements in the formation of the pathology and its complications [10].

We have studied the activity of MAO in healthy people and patients with MS, during the observation it was found that the lowest functional activity of MAO in patients with MS.

Our results indicate an increased intensification of lipid peroxidation processes in MS.

Conclusion

A comprehensive study of patients with metabolic syndrome showed significant disorders of the sympathetic-adrenal system and metabolism of biogenic amines, which is expressed in increased urinary excretion of free and conjugated forms of adrenaline and norepinephrine, and therefore early correction is necessary to prevent the development of complications.

In the metabolic syndrome, there is a pronounced decrease in the activity of the key catecholamine deamination enzyme (MAO). This leads to prolonged toxic effects of catecholamines on the myocardium.

In the metabolic syndrome, there is a significant activation of lipid peroxidation products, which is of great interest in identifying the mechanism of development of the metabolic syndrome.

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